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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,976	10/20/2003	Ileana Gabriela Sanchez De Rubio	491332000600	8662

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EXAMINER

JOIKE, MICHELE K

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 02/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/687,976	SANCHEZ DE RUBIO ET AL.	
	Examiner	Art Unit	
	Michele K. Joike, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☒ Claim(s) 21 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04/30/04 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Priority

This application repeats a substantial portion of prior Application PCT/BR02/00057, filed April 19, 2002, and adds and claims additional disclosure not presented in the prior application. Since this application names an inventor or inventors named in the prior application, it may constitute a continuation-in-part of the prior application. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78. This relationship between the instant application and the parent application(s) must be recited, i.e. this application is a continuation-in-part of PCT/BR02/00057, filed April 19, 2002.

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Brazil on April 19, 2001. It is noted, however, that applicant has not filed a certified copy of the Brazil application as required by 35 U.S.C. 119(b).

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: it does not state that the person making the oath or declaration believes the named inventor or inventors to be the original and **first** inventor or inventors of the subject matter which is claimed and for which a patent is sought.

Drawings

The drawings are objected to because vector p1-9 states that it contains 6500 b.p., however, the parent vector, Ylp352ssh, contains 4300 b.p., and a 2100 b.p. fragment was ligated into it. The new vector, p1-9, should contain only 6400 b.p.. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities: The specification is replete with spelling errors. For example, p. 1, 4th paragraph has "trancated", instead of truncated. Page 2, 3rd paragraph has "*cerevisia*", "specer" and "ot", instead of *cerevisiae*, spacer, and to.

Appropriate correction is required.

Claim Objections

Claims 1, 2, 4, 5, and 21 are objected to because of the following informalities: The claims contain spelling or grammatical errors. Claims 2 and 4 contain spelling errors. Claim 1 contains an extra "NTS1". Claim 5 contains an extra period. In claim 21, *cerevisiae* is capitalized. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5 and 10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that vectors p1-9, p1-9g18, pA-4, and pGG are required to practice the invention. As such, the vectors must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the vectors. In the instant case, the process to generate the vectors that is disclosed in the specification does not appear to be repeatable, nor does it appear the vectors are readily available to the public.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that:

- a) during the pendency of the application, access to the invention will be afforded to the

Commissioner upon request;

- b) all restrictions upon availability to the public will be irrevocably removed upon the granting of the patent;

- c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request for the enforceable life of the patent, whichever is longer;

- d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and

- e) the deposit will be replaced if it should ever become inviable.

Failure to make one of the preceding indications in response to this Office Action will result in the rejection being maintained in either a second Non-Final or a Final rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The terms "functional variations" and "functional modifications" in claim 5 is a relative term which renders the claim indefinite. The term "functional" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6, 11, 12, 14, and 16-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Kobayashi et al.

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Applicants teach a vector comprising a 5S rDNA gene, an NTS1 spacer, an NTS2 spacer and a DNA sequence of interest. The vector could also comprise an antibiotic resistance gene, conferring resistance to ampicillin, tetracycline or G418. They also teach a yeast cell transformed with said vector, wherein the yeast cell is a laboratory strain, phototrophic strain, industrial strain, or wild-type strain. Applicants teach a method of transforming the above vector and expressing the DNA sequence of interest with the transformant being stable for more than 40 generations, and the vector being integrated into chromosomal rDNA.

Kobayashi et al (Mol. and Cell Biol. 21: 136-147, 2001, specifically Fig. 1, Table 1, Material & Methods, 4th paragraph and Results section, 1st paragraph) teach a vector, pRDN-hyg 1, comprising 5S rDNA, NTS1, NTS2, *hyg 1* gene and *amp*. They also teach this vector transformed into a wild type yeast strain, with the transformant being stable for about 45 generations of growth. They also teach pRDN-hyg 1 integrated into chromosomal rDNA. As such, Kobayashi et al anticipate every aspect of the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. in view of Fincham.

Applicants claim a vector comprising a 5S rDNA gene, an NTS1 spacer, an NTS2 spacer and a DNA sequence of interest. The vector also comprises a glycol-amylose gene expression cassette of *Aspergillus awamory*.

Kobayashi et al (Mol. and Cell Biol. 21: 136-147, 2001, specifically Fig. 1, Table 1, Material & Methods, 4th paragraph and Results section, 1st paragraph) teach a vector, pRDN-hyg 1, comprising 5S rDNA, NTS1, NTS2, *hyg 1* gene and *amp*. They also teach this vector transformed into a wild type yeast strain. They do not teach using a glycol-amylose gene expression cassette.

Fincham (Microbiol. Reviews, 53: 148-170, 1989, specifically p. 165-166) teaches a glucoamylase gene expression cassette of *Aspergillus awamori*.

The ordinary skilled artisan, desiring to use a glucoamylase gene expression cassette of *Aspergillus awamori* would have been motivated to combine the teachings of Kobayashi et al of a vector, pRDN-hyg 1, comprising 5S rDNA, NTS1, NTS2, *hyg 1* gene and *amp* with the teachings of Fincham, of a glucoamylase gene expression cassette, because Fincham teaches that glucoamylase is important for disposing of plant waste. It would have been obvious to one of ordinary skill in the art to use a glucoamylase gene expression cassette of *Aspergillus awamori* because polysaccharide-degrading enzymes are important in the food industry. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said

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skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 3 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. in view of Mallet et al.

Applicants claim a vector comprising a 5S rDNA gene, an NTS1 spacer, an NTS2 spacer and a DNA sequence of interest. The vector also comprises an antibiotic resistance gene, G418.

Kobayashi et al (Mol. and Cell Biol. 21: 136-147, 2001, specifically Fig. 1, Table 1, Material & Methods, 4th paragraph and Results section, 1st paragraph) teach a vector, pRDN-hyg 1, comprising 5S rDNA, NTS1, NTS2, *hyg 1* gene and *amp*. They also teach this vector transformed into a wild type yeast strain. They do not teach using a geneticin resistance gene.

Mallet et al (Yeast 12:1351-1357, 1996, specifically p. 1354, 2nd column) teach a plasmid conferring geneticin (G418) resistance.

The ordinary skilled artisan, desiring to use antibiotic resistance as a selection method would have been motivated to combine the teachings of Kobayashi et al of a vector, pRDN-hyg 1, comprising 5S rDNA, NTS1, NTS2, *hyg 1* gene and *amp* with the teachings of Mallet et al, of a plasmid conferring geneticin (G418) resistance because Mallet et al teach that using a gene conferring geneticin resistance is beneficial because it offers selection irrespective of the genetic background (p. 1356, last paragraph). It would have been obvious to one of ordinary skill in the art to use a G418 resistance gene because it can be used in any strain. Given the teachings of the prior art and the

level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 4 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. in view of Fincham and further in view of Mallet et al.

Applicants claim a vector comprising a 5S rDNA gene, an NTS1 spacer, an NTS2 spacer and a DNA sequence of interest. The vector also comprises a glycol-amylase gene expression cassette of *Aspergillus awamory* and a gene conferring geneticin (G418) resistance.

Kobayashi et al (Mol. and Cell Biol. 21: 136-147, 2001, specifically Fig. 1, Table 1, Material & Methods, 4th paragraph and Results section, 1st paragraph) teach a vector, pRDN-hyg 1, comprising 5S rDNA, NTS1, NTS2, *hyg 1* gene and *amp*. They do not teach using a glycol-amylase gene expression cassette or a plasmid conferring geneticin (G418) resistance.

Fincham (Microbiol. Reviews, 53: 148-170, 1989, specifically p. 165-166) teaches glucoamylase gene expression cassette of *Aspergillus awamori*.

Mallet et al (Yeast 12:1351-1357, 1996, specifically p. 1354, 2nd column) teach a plasmid conferring geneticin (G418) resistance.

The ordinary skilled artisan, desiring to use a vector with a glucoamylase gene expression cassette of *Aspergillus awamori* and geneticin (G418) resistance gene would have been motivated to combine the teachings of Kobayashi et al of a vector, pRDN-hyg 1, comprising 5S rDNA, NTS1, NTS2, *hyg 1* gene and *amp* with the

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teachings of Fincham, of a glucoamylase gene expression cassette and Mallet et al teaching a plasmid conferring geneticin (G418) resistance, because Fincham teaches that glucoamylase is important for disposing of plant waste and Mallet et al teach that using a gene conferring geneticin resistance is beneficial because it offers selection irrespective of the genetic background. It would have been obvious to one of ordinary skill in the art to use a glucoamylase gene expression cassette of *Aspergillus awamori* because polysaccharide-degrading enzymes are important in the food industry and a G418 resistance gene because it can be used in any strain. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. in view of Fujiwara.

Applicants claim a vector comprising a 5S rDNA gene, an NTS1 spacer, an NTS2 spacer and a DNA sequence of interest.

Kobayashi et al (Mol. and Cell Biol. 21: 136-147, 2001, specifically Fig. 1, Table 1, Material & Methods, 4th paragraph and Results section, 1st paragraph) teach a vector, pRDN-hyg 1, comprising 5S rDNA, NTS1, NTS2, *hyg 1* gene and *amp*. They do not teach using a gene encoding an enzyme as the DNA sequence of interest.

Fujiwara (J. of Bioscience and Bioengineer. 94:518-525, 2002, Abstract) teaches thermostable enzymes.

The ordinary skilled artisan, desiring to use an enzyme as the DNA sequence of interest would have been motivated to combine the teachings of Kobayashi et al of a vector, pRDN-hyg 1, comprising 5S rDNA, NTS1, NTS2, *hyg 1* gene and *amp* with the teachings of Fujiwara, of thermostable enzymes because the DNA sequence of interest in claim 13 is not specific for a particular enzyme and could code for any one of a number of enzymes, and because Fujiwara teaches that enzymes are versatile tools for sustainable development in industry and have important environmental benefits (section I.) It would have been obvious to one of ordinary skill in the art to use a thermostable enzyme because the detergent industry needs enzymes to work under extreme conditions. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. in view of Fincham.

Applicants claim a vector comprising a 5S rDNA gene, an NTS1 spacer, an NTS2 spacer and a DNA sequence of interest and transforming the vector by homologous recombination.

Kobayashi et al (Mol. and Cell Biol. 21: 136-147, 2001, specifically Fig. 1, Table 1, Material & Methods, 4th paragraph and Results section, 1st paragraph) teach a vector, pRDN-hyg 1, comprising 5S rDNA, NTS1, NTS2, *hyg 1* gene and *amp*. They do not teach transforming by homologous recombination.

Fincham (Microbiol. Reviews, 53: 148-170, 1989, specifically p. 159, 161-162 and p. 163-164) teaches homologous recombination in *S. cerevisiae*.

The ordinary skilled artisan, desiring to use homologous recombination for transformation would have been motivated to combine the teachings of Kobayashi et al of a vector, pRDN-hyg 1, comprising 5S rDNA, NTS1, NTS2, *hyg 1* gene and *amp* with the teachings of Fincham, of homologous recombination in *S. cerevisiae* because Fincham teaches that homologous recombination is a useful technique for gene disruption or gene replacement. It would have been obvious to one of ordinary skill in the art to use homologous recombination because a fruitful application of gene replacement by homologous recombination is useful in analysis of upstream regulatory elements. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. in view of Wai et al.

Applicants claim a vector comprising a 5S rDNA gene, an NTS1 spacer, an NTS2 spacer and a DNA sequence of interest and integrating the vector into chromosomal rDNA of a yeast cell.

Kobayashi et al (Mol. and Cell Biol. 21: 136-147, 2001, specifically Fig. 1, Table 1, Material & Methods, 4th paragraph and Results section, 1st paragraph) teach a vector,

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pRDN-hyg 1, comprising 5S rDNA, NTS1, NTS2, *hyg 1* gene and *amp*. They do not teach integration of the vector into chromosomal rDNA of a yeast cell.

Wai et al (Nuc. Acid Res., 28: 3524-3534, 2000, specifically Abstract and Material & Methods) teach integration of a vector into chromosomal rDNA in *S. cerevisiae*.

The ordinary skilled artisan, desiring to integrate a vector into chromosomal rDNA in yeast would have been motivated to combine the teachings of Kobayashi et al of a vector, pRDN-hyg 1, comprising 5S rDNA, NTS1, NTS2, *hyg 1* gene and *amp* with the teachings of Wai et al, of integrating a vector into chromosomal rDNA in *S. cerevisiae* because Wai et al teach that integrating a vector into chromosomal rDNA makes it possible to assess expression of rDNA by measuring the ability of synthesized rRNA to support cell growth as well as by measuring the actual rRNA synthesized rather than by use of reporter mini-rDNA genes. Important promoter elements can also be identified using this system. It would have been obvious to one of ordinary skill in the art to use chromosomal integration because any mutational changes of rDNA can be examined. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

Claim 21 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.


No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike, Ph.D. whose telephone number is 571-272-5915. The examiner can normally be reached on M-F, 8:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michele K Joike, Ph.D.
Examiner
Art Unit 1636


DAVID GUZO
PRIMARY EXAMINER
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